REMARKS

Status of the Claims

Claims 1-51 are pending in the present application. Claims 1-19 and 32-51 are withdrawn as directed to a non-elected invention or a non-elected species. Claims 20-31 are under examination. Claims 21, 24, 27, and 30 are canceled. Claims 52 and 53 are new. Claims 20, 22, 23, 25, 26, 28, 29, and 31 are amended to define particular aspects of the invention. The claims are canceled or amended without prejudice or disclaimer. Applicants reserve the right to claim the canceled subject matter in one or more divisional or continuation applications. Independent claims 20 and 26, as amended, are directed to a method for treating arthritis (claim 20) or a method for promoting the growth of articular chondrocytes (claim 26), comprising administering a C-type natriuretic peptide (CNP) or a derivative thereof to a patient in need thereof, wherein the CNP or the derivative is selected from the CNP or specific peptide derivatives thereof, as described. Support for the amendments to independent claims 20 and 26 is found throughout the specification as originally filed including, *e.g.*, in original claims 21-24, original claims 27-30 and on page 4, lines 21-22, page 19, line 5 to page 21, line 24. Dependent claims 22, 23, 28, and 29 are amended to specify that the CNP or the derivative thereof is CNP-22 of SEQ ID NO: 1 (claims 22 and 28) or CNP-53 of SEQ ID NO: 2 (claims 23 and 29). Support for these elements is found throughout the specification as originally filed including, *e.g.*, in original claims 21-23 and 27-29. Claims 25 and 31 are amended to specify that the method further comprises administering at least one nonsteroidal anti-inflammatory drug to the patient. Support for this amendment is found throughout the specification as originally filed including, *e.g.*, on page 6, lines 13-14. New claims 52 and 53 specify that the nonsteroidal anti-inflammatory drug is indomethacin. Support for new claims 52 and 53 is found throughout the specification as originally filed including, *e.g.*, on page 9, line 24 and page 25, lines 5-11.

Objections to the Specification

The title of the present application is objected to as allegedly non-descriptive, *see* Office Action, issued June 27, 2008, page 3, (hereinafter "Office Action"). The Title has been amended to "A METHOD OF TREATING ARTHRITIS AND PROMOTING GROWTH OF

ARTICULAR CHONDROCYTES." Accordingly, Applicants believe the objection is overcome and should be withdrawn.

The Examiner also objects to the specification for failing to specify that the instant application is the national phase of PCT International Application No. PCT/JP05/06831 filed on March 31, 2005 under 35 U.S.C. § 371, *see* Office Action, page 4. Applicants have amended the specification according to the Examiner's suggestion and to further indicate that the present application also claims priority under 35 U.S.C. § 119(a) of Patent Application No. 2004/107924, filed in Japan on March 31, 2004. Based upon the foregoing, Applicants respectfully request withdrawal of the objection.

Objection to the Oath/Declaration

The Examiner states that the oath or declaration is defective because the specification to which the oath or declaration is directed is not adequately identified. Specifically, the Examiner states that the declaration filed on September 29, 2006, is missing a check mark in the box that indicates that the instant application was filed as a PCT International Application, *see* Office Action, page 4. Applicants will provide a new declaration in a supplementary amendment as the Examiner requests.

Objections to the Claims

Claims 20 and 21 are objected to for using abbreviations, *i.e.*, GC-B (claim 20) and CNP (claim 21). Claim 21 is canceled. Accordingly, the objection is moot in regard to this claim. Claim 20 is amended to specify "a guanyl cyclase (GC-B)-activating peptide," and "a C-type natriuretic peptide (CNP)." Accordingly, the objection is overcome and Applicants respectfully request withdrawal of the objections.

Claims 22 and 29 are objected to because it is allegedly unclear whether the CNP is from a single mammal or from multiple mammals simultaneously. Claims 22 and 29 are amended to specify that the CNP or the derivative thereof is CNP-22 of SEQ ID NO:1 (claim 22) or CNP-53 of SEQ ID NO:2 (claim 29). Accordingly, the objectionable phrase is canceled and Applicants respectfully request the objections be withdrawn.

Claim 26 is objected to because the word "chondrocyte" should allegedly be plural. Claim 26 is amended to expedite prosecution and specifies "chondrocytes." Accordingly, Applicants respectfully request the objection be withdrawn.

Issues Under 35 U.S.C. § 101

Claims 20-24 and 26-30 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. Specifically, the Examiner asserts that the claims are directed to methods that include naturally occurring *in vivo* activation of guanylyl cyclase B by its natural ligand, C-type natriuretic peptide, and do not require the intervention of man because the claims allegedly fail to specify method steps, *see* Office Action, pages 4-5. Claims 21 and 24 are canceled. Accordingly, the rejection is moot in regard to these claims.

Independent claims 20 and 26, as amended, are directed to a method for treating arthritis (claim 20), or promoting the growth of articular chondrocytes (claim 26) comprising administering a C-type natriuretic peptide (CNP) or a derivative thereof to a patient in need thereof, wherein the CNP or the derivative is selected from the group consisting of CNP-22 of SEQ ID NO: 1, CNP-53 of SEQ ID NO: 2, a guanyl cyclase (GC-B)-activating peptide having the amino acid sequence of SEQ ID NO: 1 in which 1 to 10 amino acids are substituted, deleted, and/or added and having an activity of activating GC-B, and a GC-B-activating peptide having the amino acid sequence of SEQ ID NO: 2 in which 1 to 10 amino acids are substituted, deleted and/or added and having an activity of activating GC-B. Support for these amendments is found as described above.

As amended, claims 20 and 26 require the intervention of man and specify the step of "administering" the described compounds to a patient in need thereof. Dependent claims 22, 23, 25, 28, and 29, and new claims 52 and 53 incorporate the elements of independent claims 20 and 26, and, accordingly, also describe the administering step. Based upon the foregoing, the claims, as amended, require the intervention of man and are not directed to non-statutory subject matter. Accordingly, Applicants respectfully request the rejection of claims 20-24 and 26-30 under 35 U.S.C. § 101 be reconsidered and withdrawn.

Issues Under 35 U.S.C. § 112, Second Paragraph

Claims 20-31 are rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Specifically, the Examiner asserts that the claims omit any positive method steps, such as a step of administration, *see* Office Action, page 5. Claims 21, 24, 27, and 30 are canceled. Accordingly, the rejection is moot in regard to these claims.

As noted above, independent claim 20, as amended, specifies the step of "administrating." Independent claim 26 is similarly amended to specify the step of "administering." Dependent claims 22, 23, 25, 28, 29, and 31, and new claims 52 and 53 incorporate the elements of independent claims 20 or 26 and, accordingly, also specify an administration step. Based upon the foregoing, Applicants believe the rejection is overcome and respectfully request the rejection be withdrawn.

Issues Under 35 U.S.C. § 112, First Paragraph

Enablement

Claims 20-24 and 26-30

Claims 20-24 and 26-30 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Specifically, the Examiner states that the claims are enabling for a method of inhibiting arthritis, wherein the arthritis is inhibited by activating guanyl cyclase B, ("G-CB") comprising administration of a mammalian or avian C-type natriuretic peptide, or a derivative that has a deletion, substitution, or addition of between 1 to 10 amino acids in the amino acid sequence of SEQ ID NO: 1 or 2, and wherein the derivative possesses the ability to bind to G-CB and increase intracellular production of cGMP. However, the Examiner asserts that the specification does not provide enablement of a method of inhibiting arthritis, wherein the arthritis is inhibited by activating GC-B, *see* Office Action, pages 5-6. In support of this assertion, the Examiner cites PCT Publication No. WO 02/074234 to Golembo *et al.*, which the Examiner indicates corresponds to Japanese Patent Publication No. 6-9688, *see* Office Action, page 8. Claims 21, 24, 27, and 30 are canceled. Accordingly, the rejection is moot in regard to these claims.

Initially, Applicants note that Japanese Patent Publication No. 6-9688, *i.e.*, Japanese Patent Publication No. 06-009688, corresponds to U.S. Patent No. 5,434,133 and European Patent No. 0497368. Applicants have cited U.S. Patent No. 5,434,133 on the Information Disclosure Statement submitted herewith.

Applicants further submit that the present application enables the pending claims. Nevertheless, in order to expedite prosecution, independent claim 20 and 26 are amended. Specifically, claims 20 and 26, as amended, are directed to a method for treating arthritis (claim 20), or a method for promoting the growth of articular chondrocytes (claim 26) comprising administering a C-type natriuretic peptide (CNP) or a derivative thereof to a patient in need thereof, wherein the CNP or the derivative is selected from the group consisting of CNP-22 of SEQ ID NO: 1, CNP-53 of SEQ ID NO: 2, a guanyl cyclase (GC-B)-activating peptide having the amino acid sequence of SEQ ID NO: 1 in which 1 to 10 amino acids are substituted, deleted, and/or added and having an activity of activating GC-B, and a GC-B-activating peptide having the amino acid sequence of SEQ ID NO: 2 in which 1 to 10 amino acids are substituted, deleted and/or added and having an activity of activating GC-B.

In addition, dependent claims 22, 23, 28, and 29 are amended to specify that the CNP or the derivative thereof is CNP-22 of SEQ ID NO: 1 (claims 22 and 28) or CNP-53 of SEQ ID NO: 2 (claims 23 and 29).

Based upon the foregoing, Applicants submit that claims 20, 22, 23, 26, 27, 28, and 29 are enabled by the present application. Reconsideration and withdrawal of the enablement rejection is respectfully requested.

Claims 25 and 31

Dependent claims 25 and 31 are also rejected for an alleged lack of enablement. Specifically, the Examiner states that the present application supports enablement of a method for treating arthritis by co-administration of a C-type natriuretic peptide ("CNP") and a non-steroidal anti-inflammatory drug ("NSAID"), however, the present application allegedly fails to support a method that requires activation of GC-B by both CNP and NSAID, *see* Office Action,

pages 9-10. The Examiner further states that the present application does not demonstrate that an NSAID, *e.g.*, indomethoacin, is actually activating GC-B, *see* Office Action, pages 9-20.

Although Applicants do not agree that the claims lack enablement support in the present application, to expedite prosecution, claims 25 and 31 are amended to specify that the method further comprises administration of at least one nonsteroidal anti-inflammatory drug to the patient. In addition, new claims 52 and 53 specify that the nonsteroidal anti-inflammatory drug is indomethacin. Based upon the foregoing amendments, Applicants submit that amended dependent claims 25 and 31 and new claims 52 and 53 are enabled by the instant application. Withdrawal of the enablement rejection is respectfully requested.

Written Description

Claims 20-31 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. Specifically, the Examiner asserts that a skilled artisan cannot envision the detailed chemical structures of the genus of GC-B activators, as specified in the instant claims, *see* Office Action, pages 11-13. The Examiner further asserts that only a mammalian or avian CNP, or a derivative that has a deletion, substitution, or addition of between 1 to 10 amino acids in the amino acid sequence of SEQ ID NOs: 1 or 2, wherein the derivative possesses the ability to bind to G-CB and increase intracellular production of cGMP, meets the written description provision of 35 U.S.C. § 112, first paragraph, *see* Office Action, page 13. Claims 21, 24, 27, and 30 are canceled. Accordingly, the rejection is moot in regard to these claims.

Although Applicants do not agree that the claims do not comply with the written description requirement, to expedite prosecution, independent claims 20 and 26 are amended to specify that the CNP or a derivative thereof is selected from CNP-22 of SEQ ID NO: 1, CNP-53 of SEQ ID NO: 2, GC-B-activating peptide having the amino acid sequence of SEQ ID NO: 1 in which 1 to 10 amino acids are substituted, deleted, and or/added and having an activity of activating GC-B, and GC-B-activating peptide having the amino acid sequence of SEQ ID NO: 2 in which 1 to 10 amino acids are substituted, deleted and/or added and having an activity of activating GC-B. Dependent claims 22, 23, 28, and 29 are also amended to specify that the CNP or the derivative thereof is CNP-22 of SEQ ID NO: 1 (claims 22 and 28) or CNP-53 of SEQ ID

NO: 2 (claims 23 and 29). Dependent claims 25 and 31 and new claims 52 and 53 incorporate the elements of independent claims 20 and 26 described above, which Applicants submit comply with the written description requirement. Based at least upon the foregoing amendments, Applicants respectfully request reconsideration and withdrawal of the written description rejection of claims 20-31.

Issues Under 35 U.S.C. § 102(b)

Claims 20-24 and 26-30 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent Publication No. 2003/0068313 to Nakao *et al* ("Nakao") and as evidenced by Mahomed *et al. American Journal of Medical Genetics*, 1998, 78:30-35 ("Mahomed"). Applicants respectfully traverse the rejection.

To anticipate a claim, the Examiner must show that the cited reference teaches every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently..., in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814, F. 2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "To establish inherency,...the missing descriptive matter must be necessarily present in the thing described in the reference,...and be so recognized by persons of ordinary skill." *In re Robertson*, 169 F. 3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F. 3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

According to the Examiner, Nakao teaches therapeutic agents for achondroplasia caused by cartilage growth inhibition resulting from mutations in the gene for fibroblast growth factor receptor 3 (FGFR3), comprising a substance activating GC-B as an active ingredient. The Examiner further states that Nakao teaches that CNP is an example of a substance that activates GC-B and is to be administered to treat achondroplasia. The Examiner cites Mahomed as evidence that 33% of patients with achondroplasia experience arthritis. Therefore, according to the Examiner, administration of CNP to patients with achondroplasia inherently inhibit arthritis from developing or worsening in these patients, *see* Office Action, pages 13-15. The Examiner

further states that Nakao teaches that CNP includes mammalian CNP-22 or CNP-53, CNP-22 of SEQ ID NO: 1, and derivatives of CNP-22, such as CNP-53, *see* Office Action, pages 14-15. The Examiner also alleges that the administration of CNP-22 to treat achondroplasia, as taught by Nakao, would also inherently promote the growth of articular chondrocytes, *see* Office Action, page 15.

In contrast to the cited references, the instant claims, as amended, are directed to a method for treating arthritis (independent claim 25), or a method for promoting the growth of articular chondrocytes (independent claim 26) comprising administering a C-type natriuretic peptide (CNP) or a derivative thereof to a patient in need thereof, wherein the CNP or the derivative is selected from the group consisting of CNP-22 of SEQ ID NO: 1, CNP-53 of SEQ ID NO: 2, a guanyl cyclase (GC-B)-activating peptide having the amino acid sequence of SEQ ID NO: 1 in which 1 to 10 amino acids are substituted, deleted, and/or added and having an activity of activating GC-B, and a GC-B-activating peptide having the amino acid sequence of SEQ ID NO: 2 in which 1 to 10 amino acids are substituted, deleted and/or added and having an activity of activating GC-B.

As noted by the Examiner, Nakao fails to expressly teach treating arthritis or promoting the growth of articular chondrocytes to a patient in need thereof by administering CNP or a derivative thereof. In addition, Applicants submit that Nakao does not inherently describe treating arthritis to a patient in need thereof. As noted above, the fact that a certain result or characteristic *may occur or be present in the prior art is not sufficient to establish the inherency* of that result or characteristic. *In re Rijckaert*, 9 F. 3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993), *emphasis added*. Patients having achondroplasia may or may not experience arthritis. In addition, the patients having achondroplasia may or may not be in need of promoting the growth of articular chondrocytes. Based upon the foregoing, Nakao, as evidenced by Mahomed, does not anticipate claims 20-24 and 26-30. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

CONCLUSION

In view of the above amendments and remarks, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Linda T. Parker, Reg. No. 46,046, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By _____

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